nephron
Clinical Practice

Nephron 2017;137(suppl1):235–250
DOI: 10.1159/000481371

Published online: September 29, 2017

# UK Renal Registry 19th Annual Report: Chapter 9 Clinical, Haematological and Biochemical Parameters in Patients on Renal Replacement Therapy in Paediatric Centres in the UK in 2015: National and Centre-specific Analyses

Alexander J Hamilton[ab], Fiona Braddon[a], Anna Casula[a], Malcolm Lewis[c], Tamara Mallett[d], Stephen D Marks[e], Mohan Shenoy[f], Manish D Sinha[g], Yincent Tse[h], Heather Maxwell[i]

[a]UK Renal Registry, Bristol, UK; [b]University of Bristol, Bristol, UK; [c]Our Lady's Children's Hospital, Crumlin, Ireland; [d]Bristol Royal Hospital for Children, Bristol, UK; [e]Great Ormond Street Hospital for Children NHS Foundation Trust, London, UK; [f]Royal Manchester Children's Hospital, Manchester, UK; [g]Evelina London Children's Hospital, London, UK; [h]Great North Children's Hospital, Newcastle Upon Tyne, UK; [i]Royal Hospital for Children, Glasgow, UK

**Keywords**

Adolescents · Biochemical variables · Blood pressure · Body mass index · Children · Dialysis · Established renal failure · Growth · Haemoglobin · Height · Hypertension · Paediatric · Quality improvement · Renal replacement therapy · Transplant · Weight · Young adults

**Summary**

- The median height z-score for paediatric patients on dialysis in 2015 was −1.8 and for those with a functioning transplant −1.2. Children transplanted before the age of 12 years improved their height z-score over the subsequent five years, whereas those older than 12 years maintained their height z-score, with all transplanted patients having a similar median height z-score after five years of starting renal replacement therapy (RRT).
- The median weight z-score for children on dialysis in 2015 was −1.1, whereas children with a functioning transplant had a near normal weight for age and sex with a median z-score of −0.2.
- Of those with data, 75% of the prevalent paediatric RRT population in 2015 had one or more 'traditional' risk factors for cardiovascular disease, with 7% having all three risk factors present.
- For the 12 centres reporting quarterly laboratory data, the median creatinine in transplant patients in 2015 was 79 μmol/L; on average, dialysis patients in 2015 had normal anaemia and acidosis parameters and evidence of secondary hyperparathyroidism, with a median parathyroid hormone (PTH) of 21 pmol/L.
- For transplant patients, 82% achieved the systolic blood pressure (SBP) standard and 93% achieved the haemoglobin standard in 2015.
- For haemodialysis patients, 63% achieved the SBP standard, 73% achieved the haemoglobin standard,

KARGER

Fax +41 61 306 12 34
E-Mail karger@karger.com
www.karger.com/nef



Alexander Hamilton
UK Renal Registry, Southmead Hospital, Southmead Road, Bristol, BS10 5NB, UK
Email: renalregistry@renalregistry.nhs.uk

76% achieved the calcium standard, 48% achieved the phosphate standard and 45% achieved the PTH standard in 2015.
- For peritoneal dialysis patients, 63% achieved the SBP standard, 75% achieved the haemoglobin standard, 70% achieved the calcium standard, 52% achieved the phosphate standard and 32% achieved the PTH standard in 2015.

## Introduction

This chapter focuses on the following variables for the prevalent paediatric dialysis and transplantation cohort on 31st December 2015:

1. The completeness of data returns to the UK Renal Registry (UKRR)
2. Anthropometric characteristics and growth
3. Cardiovascular risk factors (CVRFs)
4. Laboratory and clinical indices, including anaemia control and biochemical findings.

Analyses of prevalent paediatric patients aged <18 years receiving renal replacement therapy (RRT) for the year 2015 and for the period 2003–2015 inclusive, are reported. A single dataset was collected for each patient per year during this time period. Where possible, analyses of incident cohorts were conducted, with centre-specific data for each paediatric nephrology centre in the UK also being provided.

## Methods

Processes for data collection for the paediatric UKRR are described in chapter 4. The data presented in this chapter relate to the annual census date of 31st December 2015.

*Standards and standardisation*

Standards are in bold text and are from the Renal Association's (2002) '*Treatment of adults and children with renal failure: standards and audit measures (third edition)*' [1], unless otherwise stated.

Where the value of clinical parameters in childhood varies with age, sex and size, data are presented as z-scores.

*Anthropometry*

***'Measures of supine length or standing height and weight should be monitored at each clinic visit. All measurements should be plotted on European reference growth charts for healthy children.'***

The reference range for height (Ht), weight (Wt) and body mass index (BMI) in childhood varies with gender and age. BMI was calculated using the formula BMI = Wt (kg)/$Ht^2$ (m). Ht and Wt were adjusted for age. To account for discrepancies in linear growth secondary to renal disease, BMI was expressed according to Ht-age, rather than chronological age. The International Obesity Taskforce definition [2] was used to define overweight and obesity; z-scores were calculated based on the British 1990 reference data for Ht and Wt [3].

*Blood pressure*

***'Blood pressure varies throughout childhood and should be maintained within two standard deviations of the mean for normal children of the same height and sex. The systolic blood pressure during peritoneal dialysis or after haemodialysis should be maintained at <90th centile for age, gender and height.'***

***'In paediatric renal transplant patients, the systolic blood pressure should be maintained at <90th percentile for age, gender and height.'***

The analyses of systolic blood pressure (SBP) in this report present the achievement of SBPs at or below the 90th percentile. Guidance for blood pressure in paediatric renal transplant patients was based on 2011 British Association for Paediatric Nephrology recommendations [4].

The reference range for SBP varies with gender, age and Ht. The data are therefore presented as z-scores based on data from the fourth report of the National High Blood Pressure Education Programme working group in the United States [5].

*Cholesterol*

The National Heart Lung and Blood Institute recommends screening for dyslipidaemias in children with chronic kidney disease (CKD)/established renal failure (ERF)/post renal transplant (deemed high risk) between the ages of two and 17 years, and defines high total cholesterol as ≥5.2 mmol/L [6]. This cut-off has been adopted for this report.

*Haemoglobin and ferritin*

Guidance on the management of anaemia in adults and children with CKD was updated and published by the National Institute for Health and Care Excellence in February 2011 (clinical guideline 114) [7]. Subsequent guidance was issued during the 2015 data collection period and uses the same haemoglobin (Hb) parameters as previously but recommends newer methods of assessing iron stores over ferritin.

***'Typically maintain the aspirational Hb range between 100 and 120 g/L for young people and children aged 2 years and older, and between 95 and 115 g/L for children younger than 2 years of age, reflecting the lower normal range in that age group.'***

Hb and ferritin were analysed using age-related laboratory reference ranges as in table 9.1.

*Calcium, phosphate and parathyroid hormone (PTH)*

***'Serum phosphate and calcium should be kept within the normal range. PTH levels should be maintained within twice the upper limit of the normal range but, contrary to adult standards, may be kept within the normal range if growth is normal.'***

**Table 9.1.** Summary of relevant biochemical clinical audit measures

| | Age (years) | | | |
|---|---|---|---|---|
| Parameter | <1 | 1–5 | 6–12 | >12 |
| Hb (g/L), NICE guideline CG 114 | Maintain 95–115 if aged <2 years | Maintain 100–120 if aged >2 years | 100–120 | 100–120 |
| Ferritin (μg/L) | 200–500 | 200–500 | 200–500 | 200–500 |
| Corrected calcium (mmol/L) | 2.24–2.74 | 2.19–2.69 | 2.19–2.69 | 2.15–2.55 |
| Phosphate (mmol/L) | 1.10–1.95 | 1.05–1.75 | 1.05–1.75 | 1.05–1.75 |
| PTH (individual centre) | Within twice the normal range<br>Levels may be maintained within normal range if growing appropriately | | | |
| Bicarbonate (mmol/L) | Reported as either within or outside centre reference range | | | |

Hb – haemoglobin; NICE – National Institute for Health and Care Excellence; PTH – parathyroid hormone

Calcium, phosphate and PTH were analysed using age-related laboratory reference ranges as in table 9.1. Individual variable data analysis has been performed per centre and nationally. It should be noted that 'normal' growth is difficult to determine in the setting of paediatric RRT.

*Bicarbonate*

***'Serum bicarbonate concentrations should be between 20 and 26 mmol/L.'***

Bicarbonate reference ranges vary by centre and are reported as within or outside the reference range as given in table 9.1.

*Cardiovascular risk factors*

A cross-sectional evaluation of the prevalence of traditional risk factors for cardiovascular disease, including hypertension, overweight/obesity and hypercholesterolaemia in children with ERF is presented. In this analysis, the prevalence of one or more CVRFs in children with ERF in the UK is shown. Evidence for the use of total cholesterol and the relationship of childhood CVRFs with adult CVRFs is available from The National Heart Lung and Blood Institute [6].

*Statistical analyses*

Annual and quarterly clinical and laboratory data have been analysed separately, with annual data being used unless stated otherwise. Data were analysed to calculate summary statistics (maximum, minimum, mean and median values in addition to standard deviation and quartile ranges). Where applicable, the percentage achieving the audit standard was also calculated. If a patient had missing data, they were excluded from the relevant analyses.

Estimated glomerular filtration rate (eGFR) was calculated using the Schwartz formula [8], using centre-specific individual correction factors submitted to the UKRR.

Longitudinal analyses of attainment of standards were also performed. These were based on a single data point per ERF patient per year collected as described previously. Caution should be exercised in the interpretation of analyses based on data items from a single annual measurement per patient. This is due to changing audit standards over time and variable data returns for previous years. Furthermore, for biochemical variables there are not only differences between assays used at different centres to consider, but also differences in the timing of the result between modalities. All analyses were performed using SAS 9.3.

## Results

### *Data completeness*

*Annual data*

Tables 9.2 and 9.3 show the completeness of annual data returns for transplant and dialysis patients for 2015.

Overall, completeness was excellent for key variables in both groups, with the larger group of transplant patients having better completeness for Ht, BMI, and SBP and the smaller group of dialysis patients having better completeness for PTH. Ferritin completeness was relatively low in transplant patients, which may reflect satisfactory graft function and anaemia control, or use of alternative methods of assessing iron stores. Reporting of therapy for anaemia remained patchy and a cholesterol value was reported to the paediatric UKRR for only half of the patients.

*Quarterly data*

Twelve centres supplied quarterly 2015 data to the UKRR. Completeness of these data is shown for transplant patients in table 9.4 and dialysis patients in table 9.5. For transplant patients, ferritin and PTH were included in quarterly returns, but were not widely used; the overall quarterly completeness for ferritin in transplant patients was 40% and for PTH was 59%.

**Table 9.2.** Percentage data completeness for transplant patients <18 years old by centre for each variable and total number of patients per centre on 31st December 2015

| | Transplant patients % completeness | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Centre | *N* | Ht | Wt | BMI | SBP | Hb | Creat | Ferr | ESA | IV iron | Chol | Bicarb | PTH | Ca | Phos |
| Bham_P* | 85 | 100.0 | 100.0 | 100.0 | 100.0 | 98.8 | 98.8 | 51.9 | 0.0 | 0.0 | 1.2 | 98.8 | 96.4 | 98.8 | 98.8 |
| Blfst_P* | 18 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 94.4 | 100.0 | 100.0 | 88.2 | 100.0 | 88.9 | 100.0 | 100.0 |
| Brstl_P* | 39 | 92.3 | 97.4 | 92.3 | 84.6 | 100.0 | 100.0 | 52.6 | 100.0 | 89.7 | 68.4 | 97.4 | 65.8 | 100.0 | 100.0 |
| Cardf_P | 23 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 95.7 | 100.0 | 100.0 | 100.0 | 100.0 |
| Glasg_P* | 42 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 67.5 | 100.0 | 100.0 | 43.9 | 100.0 | 100.0 | 100.0 | 100.0 |
| L Eve_P* | 82 | 97.6 | 98.8 | 97.6 | 98.8 | 98.8 | 93.9 | 95.1 | 100.0 | 100.0 | 81.5 | 93.9 | 93.9 | 93.9 | 93.9 |
| L GOSH_P* | 150 | 100.0 | 100.0 | 100.0 | 99.3 | 100.0 | 100.0 | 92.0 | 88.0 | 87.3 | 61.9 | 98.7 | 98.0 | 100.0 | 100.0 |
| Leeds_P* | 68 | 89.7 | 100.0 | 89.7 | 97.1 | 100.0 | 100.0 | 79.4 | 100.0 | 100.0 | 41.8 | 100.0 | 88.2 | 100.0 | 100.0 |
| Livpl_P | 43 | 93.0 | 93.0 | 93.0 | 93.0 | 93.0 | 93.0 | 73.8 | 90.7 | 93.0 | 72.1 | 93.0 | 7.1 | 93.0 | 93.0 |
| Manch_P* | 61 | 98.4 | 100.0 | 98.4 | 100.0 | 100.0 | 100.0 | 73.8 | 96.7 | 96.7 | 16.4 | 100.0 | 100.0 | 100.0 | 100.0 |
| Newc_P* | 27 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 92.6 | 100.0 | 100.0 | 88.0 | 100.0 | 88.9 | 100.0 | 100.0 |
| Nottm_P* | 69 | 86.6 | 88.1 | 86.6 | 82.4 | 92.5 | 92.7 | 82.8 | 92.7 | 1.5 | 84.1 | 92.7 | 75.8 | 92.7 | 92.7 |
| Soton_P | 25 | 96.0 | 100.0 | 96.0 | 88.0 | 100.0 | 100.0 | 88.0 | 96.0 | 96.0 | 64.0 | 100.0 | 100.0 | 100.0 | 100.0 |
| **UK** | **732** | **96.4** | **98.2** | **96.4** | **96.2** | **98.6** | **98.1** | **79.9** | **84.3** | **75.2** | **56.3** | **97.7** | **87.3** | **98.1** | **98.1** |

Ht – height; Wt – weight; BMI – body mass index; SBP – systolic blood pressure; Hb – haemoglobin; Creat – creatinine; Ferr – ferritin; ESA – erythropoietin stimulating agent; IV – intravenous; Chol – cholesterol; Bicarb – bicarbonate; PTH – parathyroid hormone; Ca – calcium; Phos – phosphate

*Denotes centre undertaking paediatric kidney transplantation

**Table 9.3.** Percentage data completeness for dialysis patients <18 years old by centre for each variable and total number of patients per centre on 31st December 2015

| | Dialysis patients % completeness | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Centre | *N* | Ht | Wt | BMI | SBP | Hb | Ferr | ESA | IV iron | Chol | Bicarb | PTH | Ca | Phos |
| Bham_P | 25 | 92.0 | 88.0 | 88.0 | 96.0 | 96.0 | 89.7 | 0.0 | 0.0 | 0.0 | 96.0 | 92.6 | 96.0 | 96.0 |
| Blfst_P | 7 | 87.5 | 100.0 | 87.5 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 62.5 | 100.0 | 100.0 | 100.0 | 100.0 |
| Brstl_P | 17 | 94.1 | 100.0 | 94.1 | 100.0 | 100.0 | 100.0 | 100.0 | 82.4 | 77.8 | 100.0 | 94.4 | 100.0 | 100.0 |
| Cardf_P | 8 | 100.0 | 100.0 | 100.0 | 87.5 | 100.0 | 100.0 | 100.0 | 100.0 | 62.5 | 100.0 | 100.0 | 100.0 | 100.0 |
| Glasg_P | 14 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 73.3 | 100.0 | 100.0 | 100.0 | 100.0 |
| L Eve_P | 18 | 11.1 | 27.8 | 11.1 | 27.8 | 88.9 | 100.0 | 100.0 | 100.0 | 63.2 | 94.4 | 94.4 | 94.4 | 94.4 |
| L GOSH_P | 29 | 93.1 | 100.0 | 93.1 | 100.0 | 100.0 | 86.7 | 86.2 | 86.2 | 62.5 | 100.0 | 100.0 | 100.0 | 100.0 |
| Leeds_P | 14 | 85.7 | 92.9 | 85.7 | 92.9 | 100.0 | 100.0 | 100.0 | 100.0 | 60.0 | 100.0 | 100.0 | 100.0 | 100.0 |
| Livpl_P | 13 | 69.2 | 84.6 | 69.2 | 84.6 | 84.6 | 78.6 | 92.3 | 76.9 | 30.8 | 61.5 | 85.7 | 92.3 | 92.3 |
| Manch_P | 30 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 55.6 | 100.0 | 100.0 | 100.0 | 100.0 |
| Newc_P | 9 | 88.9 | 88.9 | 88.9 | 88.9 | 100.0 | 100.0 | 100.0 | 100.0 | 90.9 | 100.0 | 100.0 | 100.0 | 100.0 |
| Nottm_P | 18 | 85.0 | 85.0 | 85.0 | 57.9 | 100.0 | 100.0 | 100.0 | 42.1 | 55.6 | 100.0 | 100.0 | 100.0 | 100.0 |
| Soton_P | 7 | 100.0 | 100.0 | 100.0 | 57.1 | 85.7 | 100.0 | 85.7 | 85.7 | 14.3 | 100.0 | 100.0 | 100.0 | 100.0 |
| **UK** | **209** | **84.9** | **89.1** | **84.4** | **85.7** | **97.2** | **95.5** | **85.2** | **77.6** | **53.8** | **96.7** | **97.2** | **98.6** | **98.6** |

Ht – height; Wt – weight; BMI – body mass index; SBP – systolic blood pressure; Hb – haemoglobin; Ferr – ferritin; ESA – erythropoietin stimulating agent; IV – intravenous; Chol – cholesterol; Bicarb – bicarbonate; PTH – parathyroid hormone; Ca – calcium; Phos – phosphate

*Growth*

*Height*

Figures 9.1 and 9.2 show that children receiving RRT were short for their age and sex and that those on dialysis were significantly shorter than those with renal transplants. The overall median z-score (shown by the dotted line) was −1.2 in the transplanted group and −1.8 in the dialysis group ($p < 0.0001$). Evelina was excluded from figure 9.2 because few Ht data for dialysis patients were reported. Figure 9.3 demonstrates that by the

**Table 9.4.** Percentage data completeness for transplant patients <18 years old by centre reporting quarterly laboratory data and total number of patients per centre on 31st December 2015

| | | Transplant patients % completeness | | | | |
|---|---|---|---|---|---|---|
| Centre | *N* | Creatinine | Hb | Calcium | Phosphate | Bicarbonate |
| Bham_P | 85 | 91.8 | 93.1 | 90.9 | 91.2 | 90.3 |
| Blfst_P | 18 | 100.0 | 98.6 | 100.0 | 100.0 | 100.0 |
| Brstl_P | 39 | 96.1 | 92.8 | 91.4 | 91.4 | 86.8 |
| Cardf_P | 23 | 96.5 | 94.1 | 96.5 | 96.5 | 96.5 |
| Glasg_P | 42 | 100.0 | 99.4 | 99.4 | 99.4 | 100.0 |
| L Eve_P | 82 | 94.3 | 71.7 | 94.3 | 94.3 | 94.3 |
| L GOSH_P | 150 | 95.2 | 94.8 | 95.2 | 94.8 | 92.9 |
| Leeds_P | 68 | 94.4 | 94.0 | 94.0 | 93.6 | 92.8 |
| Manch_P | 61 | 100.0 | 99.5 | 100.0 | 100.0 | 100.0 |
| Newc_P | 27 | 88.0 | 84.0 | 88.0 | 88.0 | 84.0 |
| Nottm_P | 69 | 86.7 | 83.8 | 85.1 | 85.9 | 84.2 |
| Soton_P | 25 | 63.6 | 58.6 | 59.6 | 59.6 | 59.6 |
| **UK** | **689** | **93.2** | **89.6** | **92.4** | **92.4** | **91.2** |

Hb – haemoglobin

**Table 9.5.** Percentage data completeness for dialysis patients <18 years old by centre reporting quarterly laboratory data and total number of patients per centre on 31st December 2015

| | | Dialysis patients % completeness | | | | | |
|---|---|---|---|---|---|---|---|
| Centre | *N* | Hb | Ferritin | Calcium | Phosphate | PTH | Bicarbonate |
| Bham_P | 25 | 91.0 | 73.0 | 92.0 | 92.0 | 83.0 | 91.0 |
| Blfst_P | 7 | 100.0 | 96.6 | 96.6 | 100.0 | 93.1 | 100.0 |
| Brstl_P | 17 | 100.0 | 84.8 | 100.0 | 100.0 | 97.0 | 100.0 |
| Cardf_P | 8 | 100.0 | 100.0 | 100.0 | 100.0 | 96.8 | 100.0 |
| Glasg_P | 14 | 100.0 | 96.4 | 98.2 | 98.2 | 92.7 | 100.0 |
| L Eve_P | 18 | 65.1 | 72.3 | 84.3 | 84.3 | 83.1 | 84.3 |
| L GOSH_P | 29 | 100.0 | 45.0 | 100.0 | 100.0 | 100.0 | 100.0 |
| Leeds_P | 14 | 96.7 | 88.5 | 95.1 | 95.1 | 93.4 | 96.7 |
| Manch_P | 13 | 96.0 | 95.2 | 96.0 | 95.2 | 96.0 | 96.0 |
| Newc_P | 9 | 97.3 | 100.0 | 100.0 | 97.3 | 100.0 | 97.3 |
| Nottm_P | 18 | 97.4 | 93.4 | 97.4 | 97.4 | 89.5 | 96.1 |
| Soton_P | 7 | 85.7 | 100.0 | 100.0 | 100.0 | 92.9 | 100.0 |
| **UK** | **179** | **94.0** | **82.0** | **96.2** | **96.1** | **93.0** | **96.1** |

Hb – haemoglobin; PTH – parathyroid hormone

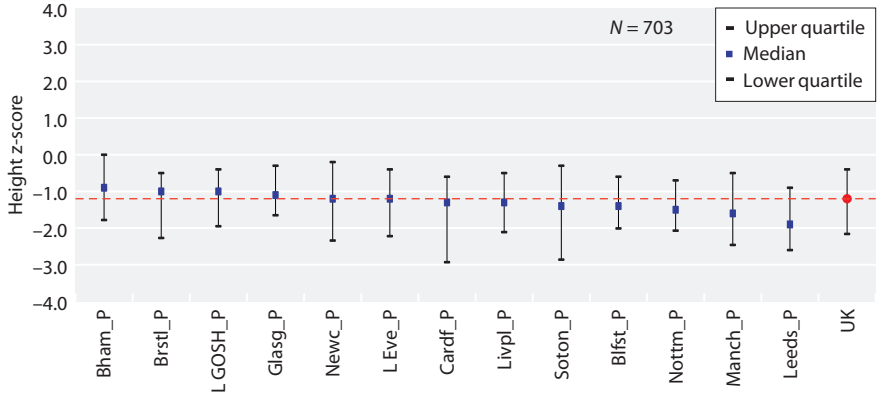


**Fig. 9.1.** Median height z-scores for transplant patients <18 years old on 31st December 2015, centre specific and national averages

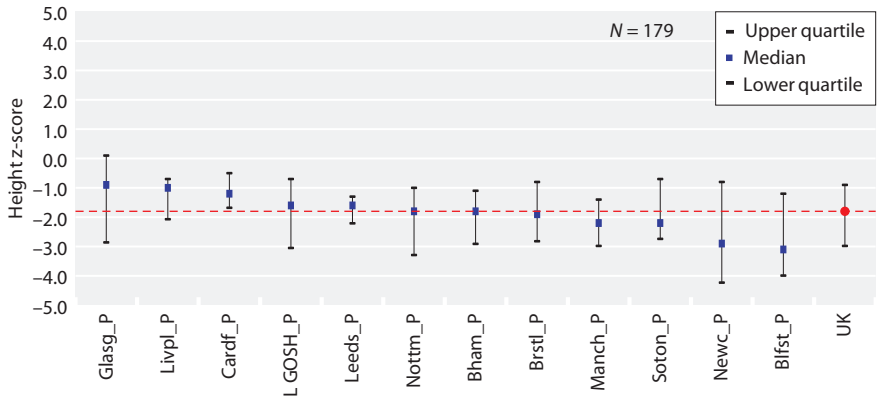


**Fig. 9.2.** Median height z-scores for dialysis patients <18 years old on 31st December 2015, centre specific and national averages

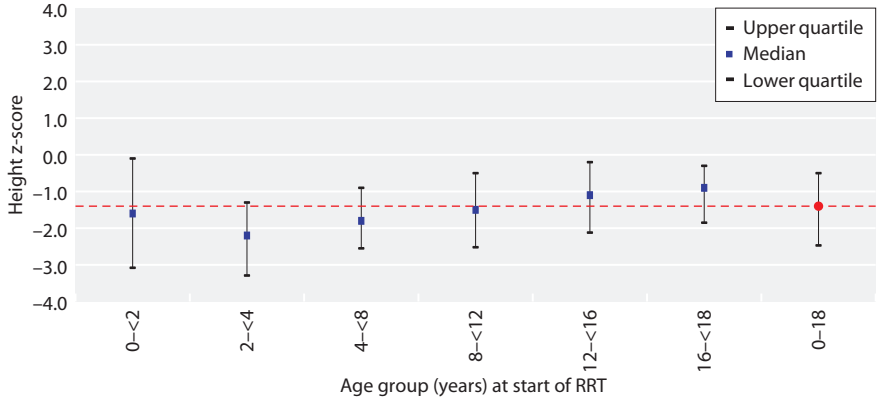


**Fig. 9.3.** Median height z-scores at start of RRT for patients <18 years old between 2003 and 2015, by age at start

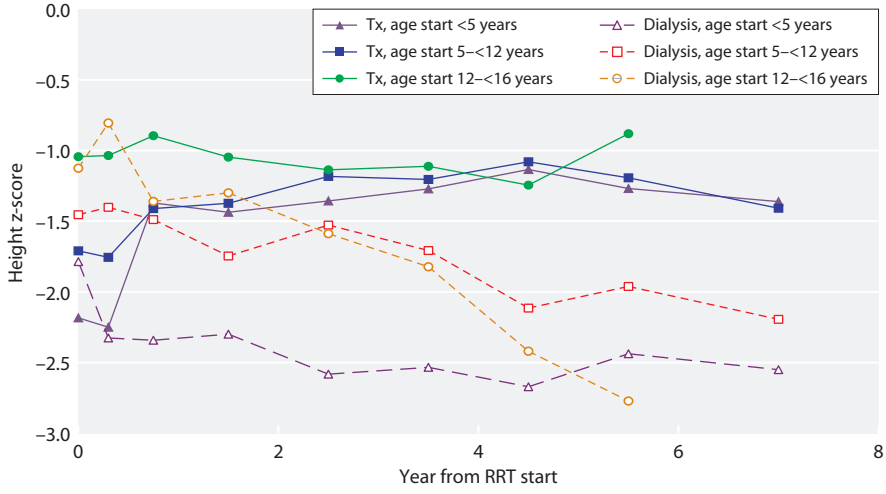


**Fig. 9.4.** Median height z-scores for patients <16 years old, by time on RRT and treatment modality

time of RRT start, children were already short for their age and sex with an overall median z-score of −1.4, with younger children aged two to eight years most affected. Figure 9.4 shows that although transplanted paediatric patients aged up to 12 years improved their Ht z-score in the first five years of starting RRT, those older than 12 years started with a better Ht z-score which was maintained. In contrast, all dialysis patients had a worsening Ht z-score over time. Poor growth was more pronounced in the oldest children, who exhibited better growth at RRT start. Due to changes in modality, groups are not strictly sequential in this analysis and because most patients received a transplant, there are small numbers of dialysis patients at five years

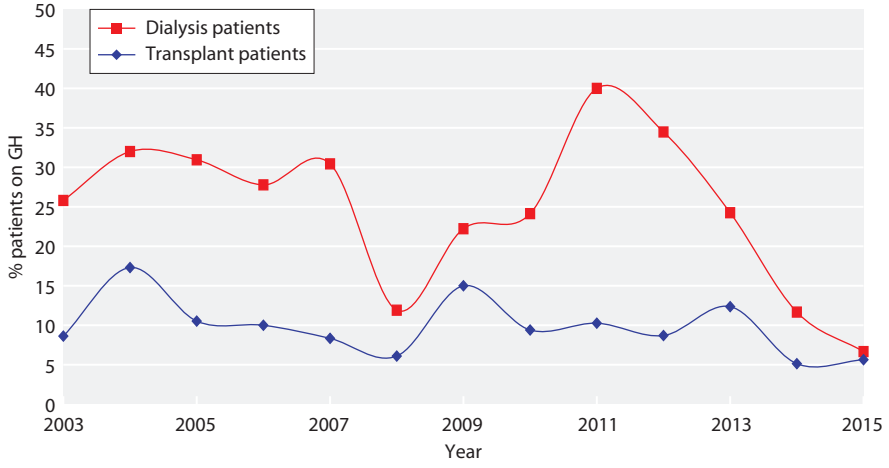


**Fig. 9.5.** Use of growth hormone in children <18 years old with a height under two SDs between 2003 and 2015

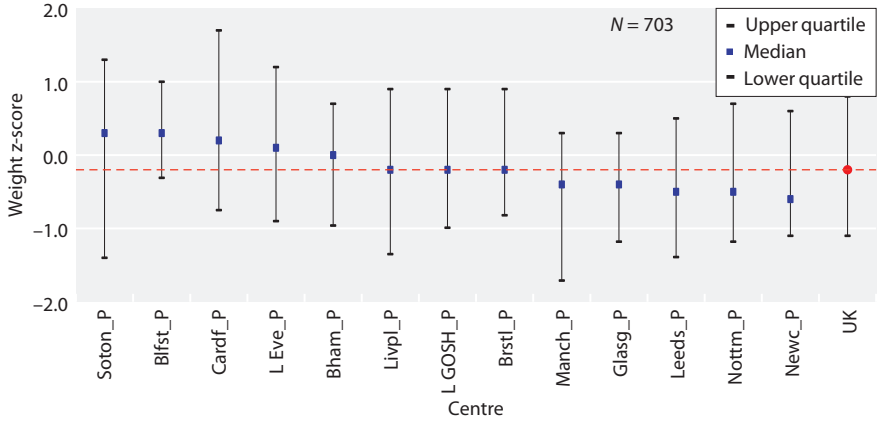


**Fig. 9.6.** Median weight z-scores for transplant patients <18 years old on 31st December 2015, centre specific and national averages

after starting RRT. Data for 16–18 year olds were omitted owing to small group numbers.

The proportion of patients aged two to 18 years with a Ht less than two standard deviations (SDs) in 2015 was much higher for those on dialysis (43.4% for haemodialysis (HD) and 34.4% for peritoneal dialysis (PD)) compared to those with a functioning transplant (27.1%), excluding patients with syndromes and those born prematurely where growth might be compromised.. Figure 9.5 shows large variation over the 13 years to 2015 in the use of growth hormone in those with a Ht less than two SDs. The proportion of patients with a Ht less than two SDs whose growth hormone status was not known is high (changing from approximately 10% in 2010 to 50% in 2011) and this limits meaningful interpretation. Average use of growth hormone for patients aged <18 years with a Ht less than two SDs since 2003 was 18.1% for dialysis patients and 7.4% for transplant patients.

*Weight*

Figures 9.6 and 9.7 show that paediatric patients receiving dialysis were significantly more underweight for age and sex than those with renal transplants. The overall median z-score was −0.2 in the transplanted group and −1.1 in the dialysis group ($p < 0.0001$). Centre level comparison for dialysis patients in particular should be avoided due to low numbers per centre.

When taking Ht into account and examining BMI rather than Wt alone, figures 9.8 and 9.9 show that BMI z-scores were mostly within the upper half of the normal range for transplant patients and spread throughout the normal range in dialysis patients. Evelina was excluded from figure 9.9 as stated above. The majority of paediatric RRT patients had a BMI within the normal range, as shown in figure 9.10.

*Cardiovascular risk factor evaluation*

*Obesity*

Figures 9.8 and 9.9 show that children with renal transplants had a significantly higher BMI for age and sex than those receiving dialysis. The overall median z-score was 1.0 in the transplanted group and 0.2 in the dialysis group ($p < 0.0001$).

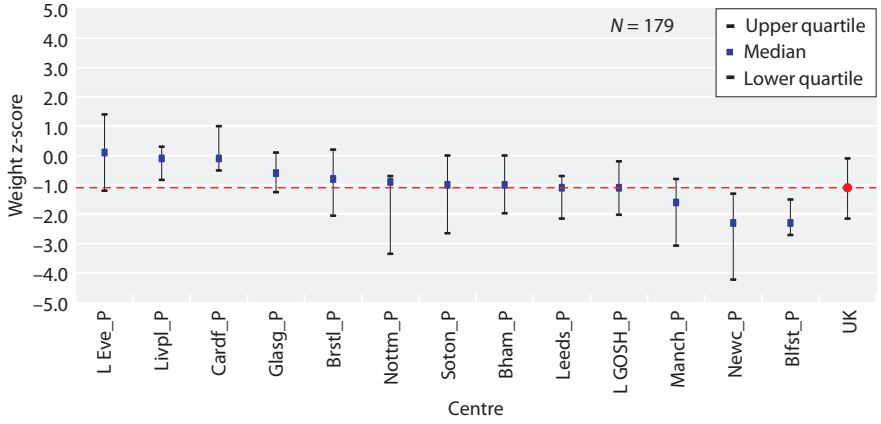


**Fig. 9.7.** Median weight z-scores for dialysis patients <18 years old on 31st December 2015, centre specific and national averages

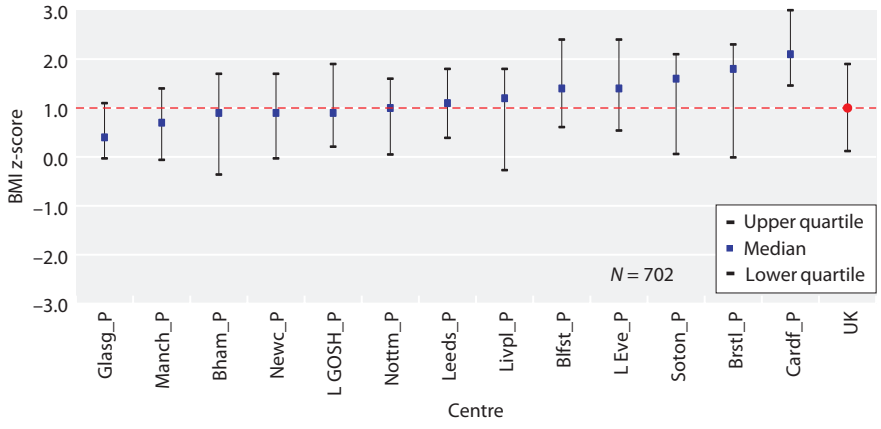


**Fig. 9.8.** Median BMI z-scores for transplant patients <18 years old on 31st December 2015, centre specific and national averages

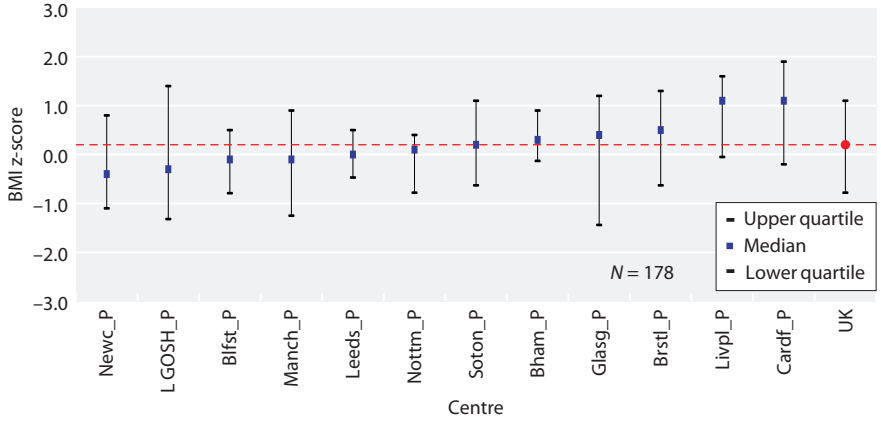


**Fig. 9.9.** Median BMI z-scores for dialysis patients <18 years old on 31st December 2015, centre specific and national averages

Figure 9.10 demonstrates higher proportions of overweight and obese children in those with renal transplants (43.6%) compared to those receiving dialysis (21.9%). There was a higher proportion of underweight children in the dialysis group (6.2%) compared to those with renal transplants (0.7%).

Of those aged 16 to <18 years, 45.1% were overweight or obese compared to 19.4% of those aged zero to under five years, but there was no significant difference by age in the transplant patient group alone. There were no statistically significant differences between proportions of those underweight, normal, overweight or obese in terms of sex, ethnicity or donor source (deceased or living).

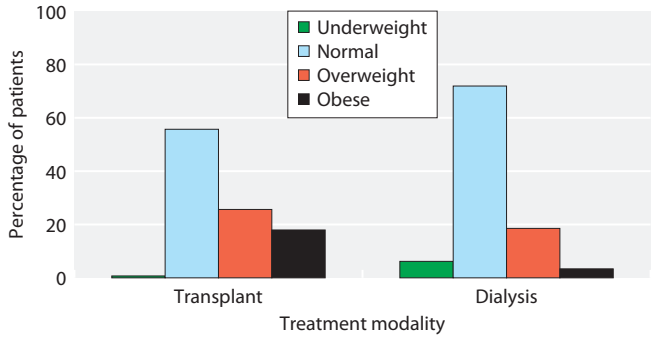


**Fig. 9.10.** BMI categorisation in children <18 years old by modality on 31st December 2015

*Hypertension*

Figures 9.11 and 9.12 show paediatric patients receiving RRT were hypertensive compared to the healthy population and those receiving dialysis had a significantly higher median SBP than those with renal transplants. There was wide inter-centre variability in median SBP z-score. The median SBP z-score was maintained at or below the 90th percentile by all centres for transplant patients and in nine centres for dialysis patients. The overall median SBP z-score was 0.5 in the transplanted group and 0.8 in the dialysis group ($p < 0.0001$). Of those aged <18 years, 81.8% of children with a functioning kidney transplant and 63.0% of those receiving dialysis had an SBP <90th percentile in 2015 (no difference between HD and PD). No comments can be made at centre level or for dialysis patient subgroups due to small patient numbers. Table 9.6 shows that there were significant differences in the percentage below the 90th percentile for SBP between different age groups, gender and RRT modality. There was no significant difference in SBP between ethnicity, HD and PD or between living and deceased donor transplants.

*Prevalence of cardiovascular risk factors*

Table 9.7 shows that the percentage of patients with no CVRFs was 24.8%, one CVRF was 40.9%, two CVRFs was 27.3% and the percentage of those with all evaluated CVRFs was 7.0%. This analysis is restricted to the 487 of 941 (51.8%) patients with complete data for all three items. Thus, of the included prevalent paediatric RRT population three quarters had one or more risk factors

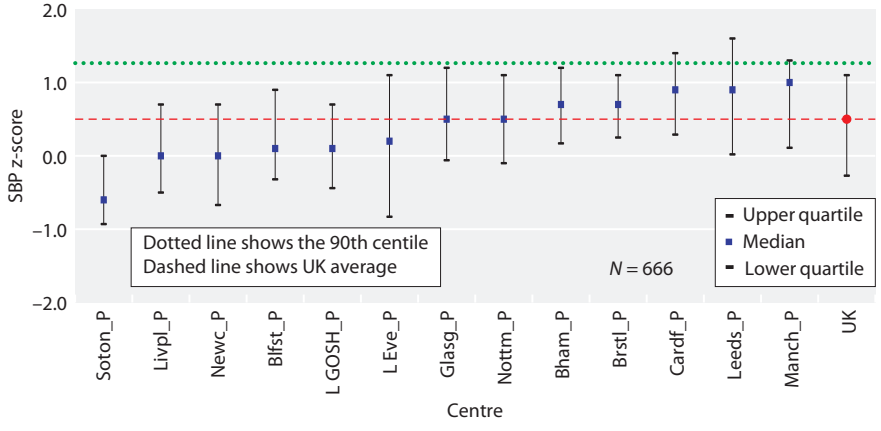


**Fig. 9.11.** Median SBP z-scores for transplant patients <18 years old on 31st December 2015, centre specific and national averages

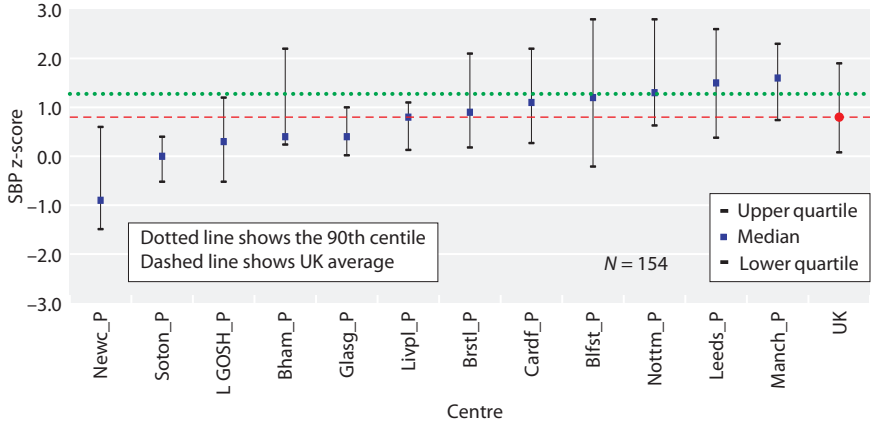


**Fig. 9.12.** Median SBP z-scores for dialysis patients <18 years old on 31st December 2015, centre specific and national averages

**Table 9.6.** Percentage of patients <18 years old achieving the standard for SBP on 31st December 2015

| | *N* | % below 90th percentile | *p*-value |
|---|---|---|---|
| **Total** | 820 | 78.3 | |
| **Age group (years)** | | | 0.001 |
| 0–<5 | 94 | 70.2 | |
| 5–<12 | 337 | 73.9 | |
| 12–<16 | 250 | 86.4 | |
| 16–<18 | 139 | 79.9 | |
| **Gender** | | | 0.04 |
| Male | 518 | 80.7 | |
| Female | 302 | 74.2 | |
| **Ethnicity** | | | 0.6 |
| Black | 31 | 83.9 | |
| Other | 65 | 75.4 | |
| South Asian | 128 | 75.8 | |
| White | 568 | 79.2 | |
| **RRT modality** | | | <0.0001 |
| Dialysis | 154 | 63.0 | |
| Transplant | 666 | 81.8 | |

for cardiovascular disease. Of those included in this analysis, 151 (31.0%) had hypertension, 214 (43.9%) were overweight/obese and 202 (41.5%) had hypercholesterolaemia. There were no statistically significant differences in number of CVRFs according to age, gender, ethnicity or modality.

*Laboratory and clinical indices – quarterly data*

Tables 9.8 and 9.10 display the median values and interquartile ranges (IQRs) for quarterly laboratory parameters for paediatric transplant and dialysis patients in 2015 by centre, with table 9.9 showing age-specific creatinine results. The total number of data points for each parameter varied depending on completeness, ranging from 2,384 data points for creatinine in transplant patients to 645 data points for ferritin in dialysis patients.

For transplant patients, these results demonstrate excellent average renal allograft function in the paediatric population, with associated good anaemia control and normal bone metabolism markers. For comparison, the median eGFR for all transplant patients (based on annual rather than quarterly data) was 61 ml/min/1.73 $m^2$ and fell with age (83 if aged <five years; 65 if aged five to <12 years; 60 if aged 12–<16 years; and 52 if aged 16–<18 years). The overall median ferritin in transplant patients was 66 μg/L (IQR 32–145) based on 40% completeness. Similarly, the overall median PTH in transplant patients was 6.9 pmol/L (IQR 4.6–10.6) based on 59% completeness.

For dialysis patients, the average Hb and ferritin were within the target range. For bone biochemistry, although average calcium and phosphate were in range, there was evidence of hyperparathyroidism with average PTH over target at more than twice the upper limit of normal, with variation between centres. Control of acidosis was also within the desired range.

*Laboratory and clinical indices – annual data*

*Haemoglobin and ferritin*

The percentage of patients aged <18 years on dialysis achieving the Hb standard in 2015 was 72.9% for those on HD and 74.5% for those on PD, compared to 92.8% for those with a renal transplant. There was no pattern by age and no comments could be made at centre level or for dialysis patients due to small patient numbers. During 2013–2015, 72.9% of dialysis patients and 92.2% of

**Table 9.7.** Frequency of number of CVRFs in prevalent RRT patients <18 years old on 31st December 2015

| Number of CV risk factors | Hypertensive | OW/Obese | Hypercholesterolaemic | *N* | % | Total % |
|---|---|---|---|---|---|---|
| 0 | No | No | No | 121 | 24.8 | **24.8** |
| 1 | Yes | No | No | 45 | 9.2 | |
| | No | Yes | No | 84 | 17.2 | **40.9** |
| | No | No | Yes | 70 | 14.4 | |
| 2 | Yes | Yes | No | 35 | 7.2 | |
| | Yes | No | Yes | 37 | 7.6 | **27.3** |
| | No | Yes | Yes | 61 | 12.5 | |
| 3 | Yes | Yes | Yes | 34 | 7.0 | **7.0** |
| *N* | 151 | 214 | 202 | | | |
| **Total %** | **31.0** | **43.9** | **41.5** | | | |

CV – cardiovascular; OW – overweight

**Table 9.8.** Median quarterly laboratory data by centre in prevalent transplant patients <18 years old on 31st December 2015

| | Transplant patients | | | | |
|---|---|---|---|---|---|
| Centre | Creatinine (μmol/L) | Haemoglobin (g/L) | Calcium (mmol/L) | Phosphate (mmol/L) | Bicarbonate (mmol/L) |
| Bham_P | 70 | 120 | 2.46 | 1.31 | 25 |
| Blfst_P | 77 | 124 | 2.47 | 1.21 | 22 |
| Brstl_P | 76 | 127 | 2.43 | 1.24 | 23 |
| Cardf_P | 65 | 126 | 2.50 | 1.32 | 23 |
| Glasg_P | 79 | 120 | 2.45 | 1.26 | 22 |
| L Eve_P | 84 | 120 | 2.46 | 1.20 | 22 |
| L GOSH_P | 81 | 124 | 2.48 | 1.49 | 25 |
| Leeds_P | 86 | 115 | 2.41 | 1.30 | 24 |
| Manch_P | 88 | 119 | 2.48 | 1.26 | 22 |
| Newc_P | 79 | 124 | 2.42 | 1.21 | 22 |
| Nottm_P | 76 | 124 | 2.43 | 1.28 | 25 |
| Soton_P | 94 | 115 | 2.50 | 1.30 | 24 |
| **UK median** | **79** | **122** | **2.46** | **1.31** | **24** |
| **IQR** | **(59–107)** | **(111–131)** | **(2.39–2.52)** | **(1.15–1.49)** | **(22–26)** |

IQR interquartile range

**Table 9.9.** Median quarterly creatinine by age group, centre and time since transplant in prevalent transplant patients <18 years old on 31st December 2015

| | Age (years) | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | 0–<5 | | 5–<12 | | 12–<16 | | 16–<18 | |
| Centre | *N* | Creatinine (μmol/L) | *N* | Creatinine (μmol/L) | *N* | Creatinine (μmol/L) | *N* | Creatinine (μmol/L) |
| Bham_P | 12 | 44 | 123 | 62 | 128 | 78 | 29 | 105 |
| Blfst_P | 5 | 46 | 52 | 84 | 10 | 57 | 2 | |
| Brstl_P | 3 | 149 | 86 | 65 | 34 | 86 | 23 | 100 |
| Cardf_P | 6 | 41 | 39 | 63 | 29 | 69 | 8 | 72 |
| Glasg_P | 5 | 38 | 61 | 60 | 49 | 87 | 41 | 104 |
| L Eve_P | 23 | 41 | 96 | 71 | 103 | 89 | 58 | 116 |
| L GOSH_P | 43 | 39 | 233 | 69 | 184 | 94 | 92 | 123 |
| Leeds_P | 20 | 46 | 82 | 67 | 89 | 95 | 46 | 102 |
| Manch_P | 13 | 46 | 109 | 64 | 53 | 97 | 35 | 114 |
| Newc_P | 4 | 54 | 23 | 47 | 31 | 80 | 30 | 93 |
| Nottm_P | 16 | 31 | 96 | 74 | 62 | 77 | 35 | 108 |
| Soton_P | 9 | 51 | 26 | 95 | 23 | 95 | 5 | 98 |
| **Total *N* and UK median** | **159** | **41** | **1,026** | **67** | **795** | **88** | **404** | **107** |
| **IQR** | | **(34–52)** | | **(53–87)** | | **(70–115)** | | **(88–135)** |
| **Time since transplantation (years)** | | | | | | | | |
| 3 months | 54 | 40 | 95 | 55 | 49 | 82 | 38 | 103 |
| 1 year | 62 | 42 | 137 | 66 | 90 | 81 | 50 | 109 |
| 2.5 years | 42 | 43 | 335 | 60 | 158 | 88 | 78 | 92 |
| 5 years | 1 | | 353 | 73 | 211 | 79 | 96 | 105 |
| ≥7 years | 0 | | 106 | 79 | 287 | 100 | 142 | 119 |

IQR interquartile range

**Table 9.10.** Median quarterly laboratory data by centre in prevalent dialysis patients <18 years old on 31st December 2015

| | Dialysis patients | | | | | |
|---|---|---|---|---|---|---|
| Centre | Hb (g/L) | Ferritin (μg/L) | Calcium (mmol/L) | Phosphate (mmol/L) | PTH (pmol/L) | Bicarbonate (mmol/L) |
| Bham_P | 111 | 283 | 2.61 | 1.71 | 10.3 | 27 |
| Blfst_P | 117 | 1272 | 2.56 | 1.57 | 17.2 | 26 |
| Brstl_P | 111 | 284 | 2.52 | 1.41 | 16.0 | 25 |
| Cardf_P | 128 | 224 | 2.61 | 1.50 | 52.2 | 25 |
| Glasg_P | 116 | 210 | 2.49 | 1.14 | 22.1 | 24 |
| L Eve_P | 104 | 382 | 2.51 | 1.40 | 24.6 | 24 |
| L GOSH_P | 128 | 337 | 2.64 | 2.01 | 17.0 | 30 |
| Leeds_P | 100 | 311 | 2.44 | 1.95 | 58.4 | 25 |
| Manch_P | 107 | 149 | 2.58 | 1.65 | 31.0 | 25 |
| Newc_P | 108 | 278 | 2.60 | 1.32 | 9.7 | 23 |
| Nottm_P | 103 | 238 | 2.54 | 1.64 | 16.3 | 27 |
| Soton_P | 85 | 150 | 2.50 | 1.50 | 6.6 | 25 |
| **UK median** | **111** | **278** | **2.55** | **1.62** | **21.0** | **26** |
| **IQR** | **(99–124)** | **(129–467)** | **(2.46–2.65)** | **(1.30–1.99)** | **(8.5–47.6)** | **(23–29)** |

Hb – haemoglobin; PTH – parathyroid hormone; IQR – interquartile range

transplant patients achieved the standard for Hb, which has remained consistent since the 2003–2006 period. The proportion of patients with a ferritin in range during 2013–2015 was 35.8% for dialysis patients and 13.4% for transplant patients. It is not possible to draw conclusions on ferritin data trends, because the data completeness for transplant patients was only 42.1% in the 2003–2006 period, but had improved to 79.0% in the 2013–2015 period. A similar improvement was also seen for dialysis ferritin data, increasing from 75.0% to 95.1% over the same time periods.

At first inspection, table 9.11 appears to show over time an increasing use of erythropoietin stimulating agents (ESAs) in transplant patients and a decrease in use of ESAs in dialysis patients. However, the amount of missing data increased from 2.1% in the 2003–2006 period to 16.0% in the most recent period for dialysis patients, and by a similar margin for the transplant patients.

**Table 9.11.** Proportion of paediatric RRT patients on ESA, by Hb attainment, across time

| Time period | Hb below standard % on ESA | Hb above standard % on ESA |
|---|---|---|
| **Transplant patients** | | |
| 2003–2006 | 21.1 | 4.2 |
| 2007–2009 | 21.4 | 5.6 |
| 2010–2012 | 20.0 | 5.7 |
| 2013–2015 | 31.9 | 3.6 |
| **Dialysis patients** | | |
| 2003–2006 | 97.1 | 93.2 |
| 2007–2009 | 95.9 | 91.0 |
| 2010–2012 | 82.9 | 81.0 |
| 2013–2015 | 87.5 | 96.1 |

Hb – haemoglobin; ESA – erythropoietin stimulating agent

Overall, figure 9.13 shows high usage of ESAs in dialysis patients without a clear difference by Hb standard, noting erratic results from 2010 when there was a reduction in data completeness. Usage of ESAs in transplant patients remained low and reasonably stable with a more discernible separation by Hb standard. Figure 9.14 further demonstrates wider variation for usage of intravenous (IV) iron for dialysis patients by Hb standard, in keeping with low completeness for past years, and low usage of IV iron in transplant patients.

*Calcium*

The percentage of patients aged <18 years on HD ($N = 108$) achieving the calcium standard in 2015 was 75.9%, with 3.7% of patients being hypocalcaemic and 20.4% being hypercalcaemic. The percentage of patients aged <18 years on PD ($N = 99$) achieving the calcium standard in 2015 was 69.7%, with 1.0% being hypocalcaemic and 29.3% being hypercalcaemic. Small cohort numbers prevent commentary at centre level or by age group.

*Phosphate*

The percentage of patients aged <18 years on HD ($N = 108$) achieving the phosphate standard in 2015

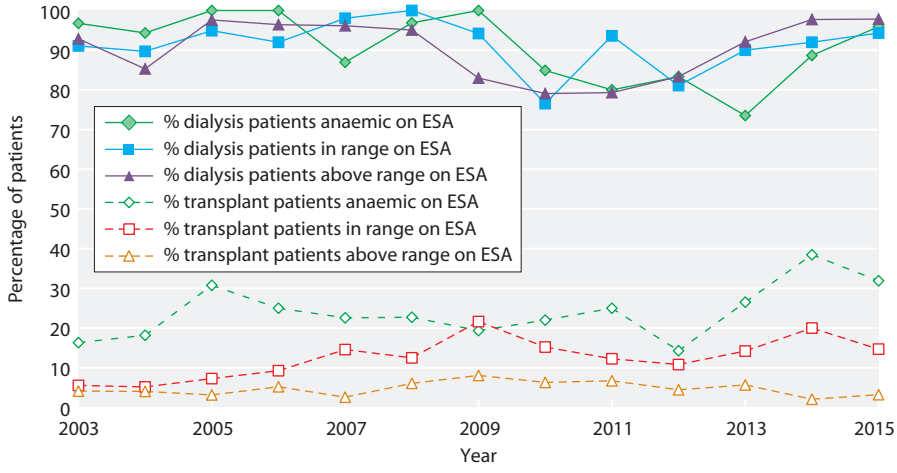


**Fig. 9.13.** The use of ESA by Hb standard and treatment modality between 2003 and 2015 in prevalent RRT patients <18 years old

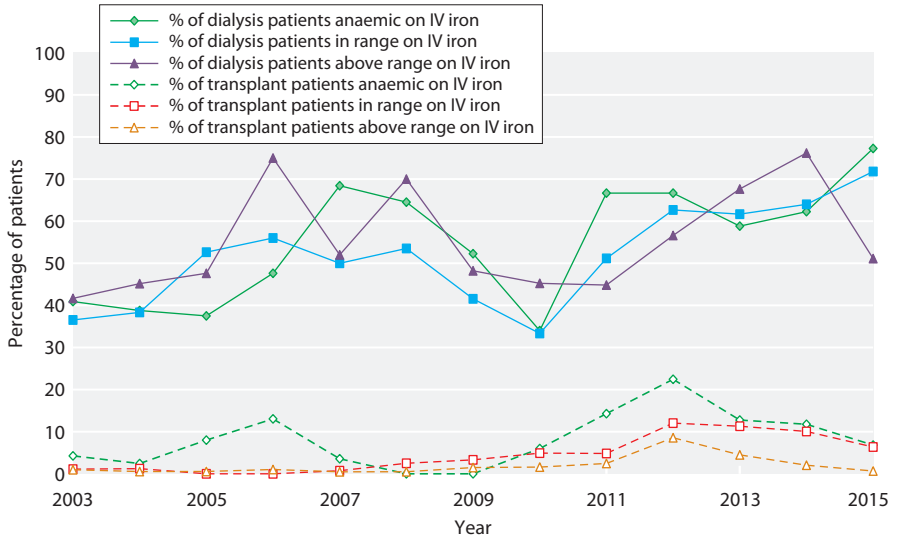


**Fig. 9.14.** The use of IV iron by Hb standard and treatment modality between 2003 and 2015 in prevalent RRT patients <18 years old

was 48.2%, with 18.5% of patients being hypophosphataemic and 33.3% being hyperphosphataemic. The percentage of patients aged <18 years on PD ($N = 99$) achieving the phosphate standard in 2015 was 51.5%, with 8.1% of patients being hypophosphataemic and 40.4% being hyperphosphataemic. Small cohort numbers prevent commentary at centre level or by age group.

*Parathyroid hormone*

The percentage of patients aged <18 years with a renal transplant ($N = 633$) achieving the PTH standard in 2015 was 80.6%, with 19.4% having hyperparathyroidism. The percentage of patients aged <18 years on HD ($N = 110$) achieving the PTH standard in 2015 was 44.6%, with 55.4% having hyperparathyroidism. The percentage of patients aged <18 years on PD ($N = 99$) achieving the PTH standard in 2015 was 32.3%, with 67.7% having hyperparathyroidism. Small cohort numbers and low completeness from some centres for transplant patients prevent commentary at centre level or by age group.

*Bicarbonate*

The percentage of patients aged <18 years with a renal transplant ($N = 714$) achieving the bicarbonate standard in 2015 was 87.0%, with 9.5% being below and 3.5% being above the standard. The percentage of patients aged <18 years on HD ($N = 105$) achieving the bicarbonate standard in 2015 was 74.3%, with 10.5% being below and 15.2% being above the standard. The percentage of patients aged <18 years on PD ($N = 98$) achieving the bicarbonate standard in 2015 was 58.2%, with 6.1% being below and 35.7% being above the standard. Small cohort numbers prevent commentary at centre level or by age group.

## Discussion

This chapter provides information describing clinical and laboratory parameters of paediatric RRT patients in the UK. This enables comparison against national standards and guidelines, assessment of quality of care and benchmarking the performance of UK tertiary paediatric nephrology centres. Data from 2015 and trends over the last 13 years have been analysed. The results and conclusions are a valuable resource for the paediatric renal community and these data account for nearly 20% of the European Paediatric Renal Registry data.

*Quarterly data*

Twelve centres provided quarterly data for analyses, an increase of two centres from the previous year. The data show excellent graft function for those with a transplant, with a breakdown by centre, age and time following kidney transplant, which may be of value for clinicians. The reporting of eGFR using quarterly data is not possible due to low completeness of Ht data, but eGFR using annual data to add to the assessment of transplant function is given. For dialysis patients, the data again demonstrate good control of anaemia and acidosis, with a median PTH of 21 pmol/L, varying widely between centres.

The ongoing challenge is to continue to work with the remaining centre to achieve quarterly returns and to improve extracts to allow new data to be loaded into a single UKRR database.

*Highlights from the 2015 data*

For core items there was very good completeness; ESA and IV iron data were limited in transplant patients perhaps because these patients tend not to be anaemic. Cholesterol and growth hormone remained the most limited variables in terms of completeness, but reporting levels were above the threshold to be used in analyses.

*Growth*

As previously reported, dialysis patients had lower median height z-scores than transplanted patients, but only constitute between a fifth and a quarter of the population. After taking completeness and IQRs into account, the median Ht z-scores were similar between centres for transplant patients (differing by a SD) and more widely spread for dialysis patients, which is not surprising given the smaller numbers per unit.

Taking into account 13 years of data, the overall median Ht z-score at RRT start for UK children was −1.4 (again with a wide IQR), demonstrating the impact of a chronic disease in childhood and suggesting there are opportunities to improve growth at earlier stages of CKD. The data show that once transplanted, patients maintained their Ht over the following five years, with those transplanted under the age of five years showing an improvement in Ht z-score since the start of RRT.

Use of growth hormone remains difficult to interpret due to a high proportion of missing data, notwithstanding the fact that there are alternative interventions to improve growth which the UKRR does not collect. Further, adjustment for situations where use of growth hormone is not recommended, such as in newly transplanted patients and in those demonstrating catch-up growth was not possible. There are plans to look at reasons why short children are not on growth hormone therapy and to look at the effects of steroid avoidance on growth in transplanted patients. A significant percentage of transplant patients were overweight or obese and steroid use may also contribute to weight gain.

While the median Wt z-score for transplant patients was near that of the healthy population, the dialysis patients were underweight, again accepting a wide IQR. As dialysis patients and transplant patients were both shorter on average than their healthy peers, this meant that transplant patients had a higher BMI than their healthy peers, with dialysis patients having relatively normal BMI. Improvements to the completeness of Ht and Wt in the quarterly data should allow growth rates to be evaluated in the future. These data will also allow evaluation of excessive Wt gain following kidney transplantation [9], identified as the most prevalent CVRF in children receiving RRT.

*Cardiovascular risk factor evaluation*

The analysis of SBP across different centres in 2015 continued to show variability both between and within centres. Statistically fewer younger patients, girls and dialysis patients achieved the SBP standard.

The data continue to show that the majority of children on RRT have CVRFs – accepting the low completeness of cholesterol data – consistent with previous reports of RRT and pre-dialysis CKD cohorts [10, 11]. Given the good completeness of other data it is interesting to speculate on the reason for lack of measurement of cholesterol in children and young people. Many clinicians are reluctant to treat mild to moderate hypercholesterolaemia due to lack of data on tolerability and efficacy of treatment in these populations.

Being overweight was the most common CVRF, suggesting that weight should be a specific target for intervention for long-term cardiovascular health of paediatric RRT patients. Whilst 80% of patients had a blood pressure below the 90th centile, there was evidence in paediatric CKD patients that suggests lower targets may be appropriate [12].

*Laboratory and clinical indices*

Annual data regarding attainment of standards for laboratory measures were similar to previous years for Hb, ferritin, calcium, phosphate, PTH and bicarbonate. There is a new NICE guideline on the treatment of anaemia in CKD and centres may be switching the way they monitor iron stores. The data collected were from before the introduction of the new guideline, which may in part explain the low figures for ferritin measurement. The new guidance should be reflected in the 2016 data.

The proportion of dialysis patients achieving the standards appears low. However, over-interpretation of single measurements of variable completeness from a small proportion of the cohort should be avoided. Once all centres are reporting quarterly biochemistry data, replacement of the assessment of achievements of standards on the quarterly median rather than the annual result will be possible.

*Future work*

The goals of the paediatric UKRR remain the reporting of quarterly data for all paediatric renal centres, improving data extracts and then combining the adult and paediatric UKRR databases.


## Acknowledgements

Thanks are expressed to Kidney Research UK and the British Kidney Patient Association whose contribution through the Tony Wing award contributed to the production of this chapter.

Conflicts of interest: the authors declare no conflicts of interest


## References


1 Renal Association standards, 3rd edition, 2002 http://www.renal.org/docs/default-source/guidelines-resources/Renal_Association_Standards_3rd_Edition_2002-2007.pdf?sfvrsn=0 (last accessed 14th November 2016).
2 Cole TJ, Flegal KM, Nicholls D, Jackson AA. Body Mass Index cut offs to define thinness in children and adolescents: international study. *BMJ* 2007; 335 (7612): 194.
3 Freeman JV, Cole TJ, Chinn S et al. Cross sectional stature and weight reference curves for the UK, 1990. Arch Dis Child 1995;73:17–24.
4 BAPN Standards for Hypertension in Paediatric Renal Transplant Recipients, 2011 http://www.renal.org/docs/default-source/special-interest-groups/bapn/clinical-standards/bapn-standards-for-hypertension-in-renal-transplant-recipients.pdf?sfvrsn=2 (last accessed 14th November 2016).
5 National High Blood Pressure Education Program Working Group on High Blood Pressure in Children and Adolescents. The Fourth Report on the Diagnosis, Evaluation, and Treatment of High Blood Pressure in Children and Adolescents. Pediatrics 2004;114(2):555–76.
6 Expert panel on integrated guidelines for cardiovascular health and risk reduction in children and adolescents: summary report. Pediatrics 2011 Dec; 128(suppl 5):S213-56. doi: 10.1542/peds.2009-2107C.
7 NICE clinical guideline 114. Anaemia management in people with chronic kidney disease. London: National Institute for Health and Clinical Excellence, 2011.
8 Schwartz GJ, Gauthier B. A simple estimate of glomerular filtration rate in adolescent boys. J Pediatr. 1985 Mar;106(3):522–6.
9 Plumb LA, Pitcher D, Tse Y, Shield JP, Inward C, Sinha MD. British Association for Paediatric Nephrology. Longitudinal changes in body mass index following renal transplantation in UK children. Nephrol Dial Transplant. 2014;29(1):196–203. doi:10.1093/ndt/gft395.
10 Wilson AC, Schneider MF, Cox C, Greenbaum LA, Saland J, White CT, Furth S, Warady BA, Mitsnefes MM. Prevalence and Correlates of Multiple Cardiovascular Risk Factors in Children with Chronic Kidney Disease. Clin J Am Soc Nephrol. 2011 Dec; 6(12):2759–65. doi: 10.2215/CJN.03010311.
11 Mitsnefes M. Cardiovascular Disease in Children with Chronic Kidney Disease. J Am Soc Nephrol 2012 23:578–585. doi: 10.1681/ASN.2011111115.
12 ESCAPE Trial Group, Wühl E, Trivelli A, Picca S, Litwin M, Peco-Antic A, Zurowska A, Testa S, Jankauskiene A, Emre S, Caldas-Afonso A, Anarat A, Niaudet P, Mir S, Bakkaloglu A, Enke B, Montini G, Wingen AM, Sallay P, Jeck N, Berg U, Caliskan S, Wygoda S, Hohbach-Hohenfellner K, Dusek J, Urasinski T, Arbeiter K, Neuhaus T, Gellermann J, Drozdz D, Fischbach M, Möller K, Wigger M, Peruzzi L, Mehls O, Schaefer F. Strict blood-pressure control and progression of renal failure in children. N Engl J Med 2009;361(17):1639–50. doi:10.1056/NEJMoa0902066.